Potential bioterrorism agent: Category A

SMALLPOX

The last naturally acquired case of smallpox in the world occurred in October 1977 in Somalia; global eradication was certified two years later by the WHO and sanctioned by the World Health Assembly (WHA) in May 1980. Except for a laboratory associated smallpox death at the University of Birmingham, England, in 1978, no cases have been identified since. All known smallpox (variola) virus stocks are held under security at the CDC, Atlanta, Georgia, or the State Research Centre of Virology and Biotechnology, Koltsovo, Novosibirsk Region, Russian Federation.

Because of the potential use of clandestine supplies of variola virus for biowarfare or bioterrorism, it is important that health care workers become familiar with the clinical and epidemiologic features of smallpox and how it was distinguished from chickenpox. Even though strains of virus used for biowarfare might have been engineered so that clinical differences may result, past experience with naturally occurring variola remains the best guide to recognition and management of an epidemic pox virus disease.

DISEASE REPORTING

In Washington:

The last case of smallpox reported in Washington State occurred in 1946.

Purpose of reporting and surveillance:

- To assist in diagnosis of cases.
- To notify appropriate agencies and mobilize necessary resources for public health response and possible criminal investigation.

Reporting requirements

- Health care providers: **immediately notifiable to Local Health Jurisdiction**
- Hospitals: **immediately notifiable to Local Health Jurisdiction**
- Laboratories: **immediately notifiable**, specimens must be tested at CDC through arrangement with DOH Communicable Disease Epidemiology
- Local health jurisdictions: **suspected or confirmed cases are immediately notifiable to DOH Communicable Disease Epidemiology: 1-877-539-4344**

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

An illness with acute onset of fever $\geq$ 101^{o} F (38.3^{o} C) followed by a rash characterized by vesicles or firm pustules in the same stage of development without other apparent cause.

Laboratory criteria for diagnosis (Level C or D laboratories only)

- Isolation of smallpox (variola) virus from a clinical specimen (level D laboratory only), or
- Polymerase chain reaction (PCR) assay identification of variola DNA in a clinical specimen (level D laboratory or approved level C laboratory only), or
- Negative stain electron microscopic (EM) identification of variola virus in a clinical specimen (level D laboratory or approved level C laboratory only).

Case definition

- Probable: A case that meets the clinical case definition, is not laboratory confirmed, but has an epidemiological link to a confirmed or probable case.
- Confirmed: A clinically compatible case that is laboratory confirmed.

A. DESCRIPTION

1. Identification

Smallpox was a systemic viral disease that generally presented with a characteristic skin eruption. Onset was sudden, with fever, malaise, headache, prostration, severe backache and occasional abdominal pain and vomiting; a clinical picture that resembled influenza. After 2 to 4 days, the fever began to fall and a deep-seated rash developed in which individual lesions containing infectious virus progressed through successive stages of macules, papules, vesicles, pustules and crusted scabs which fell off after three to four weeks. The lesions were first evident on the face and extremities and subsequently on the trunk-the so-called centrifugal rash distribution-and were at the same stage of development in a given area.

Two epidemiologic types of smallpox were recognized during the 20th century: variola minor (alastrim), which had a case fatality rate of less than 1% and variola major (ordinary) with a fatality rate among unvaccinated populations of 20-40% or more. Fatalities normally occurred between the 5th and 7th day, occasionally as late as the 2nd week. Less than 3% of variola major cases experienced fulminating disease with a severe prodrome, prostration, and bleeding into the skin and mucous membranes; such hemorrhagic cases were rapidly fatal. The usual rash did not appear and the disease might have been confused with severe leukemia, meningococcemia or idiopathic thrombocytopenic purpura.

In previously vaccinated persons, the rash was significantly modified to the extent that only a few highly atypical lesions might be seen. Generally the prodromal illness was not modified but the stages of the lesions were accelerated with crusting by the 10th day.

Most frequently smallpox was confused with chickenpox in which the skin lesions commonly occur in successive crops with several stages of maturity at the same time. The chickenpox rash is more abundant on covered than on exposed parts of the body; the rash is centripetal rather than centrifugal. Smallpox was indicated by a clear-cut prodromal illness; by the appearance of all lesions more or less simultaneously when the fever broke; by the similarity of appearance of all lesions in a given area rather than successive crops; and by more deep-seated lesions, which often involved sebaceous glands and scarring of the pitted lesions. By contrast, the chickenpox lesions are superficial. Smallpox lesions were virtually never seen at the apex of the axilla.

Outbreaks of variola minor (alastrim) appeared in the late 19th century. Although the rash was like that in ordinary smallpox, patients generally experienced less severe systemic reactions, and hemorrhagic cases were virtually unknown. Although the last cases of smallpox in Somalia in the late 1970s were classified as variola minor, DNA studies indicated that the virus was more like that of variola major than true alastrim virus, which suggested that this was an attenuated variola major. Laboratory confirmation was by isolation of the virus on chorioallantoic membranes or tissue culture from the scrapings of lesions, from vesicular or pustular fluid, from crusts, and sometimes from blood during the febrile preeruptive stage. A rapid provisional diagnosis was often possible by electron microscopy or the immunodiffusion technique. Now these methods would be superseded by more rapid and accurate PCR methods.

2. Infectious Agent

Variola virus, a species of Orthopoxvirus. Mapping of endonuclease cleavage sites of several strains of variola has been done, and the complete DNA sequences of two major strains are published.

3. Worldwide Occurrence

Formerly a worldwide disease; no known humans cases since 1978.

4. Reservoir

Officially, only in designated freezers in the US and in Russia.

5. Mode of Transmission

The secondary attack rate among unvaccinated populations was about 50% depending on the outbreak. If used in biowarfare, the agent would most likely be disseminated in an aerosol cloud.

6. Incubation period

From 7-19 days; commonly 10-14 days to onset of illness and 2-4 days more to onset of rash.

7. Period of communicability

From the time of development of the earliest lesions to disappearance of all scabs; about 3 weeks. The patient is most contagious during the preeruptive period by aerosol droplets from oropharyngeal lesions.

8. Susceptibility and resistance

Susceptibility among the unvaccinated is universal.

B. METHODS OF CONTROL

Control of smallpox is based on immunization with vaccinia virus. Should a nonvaricella, smallpox-like case be suspected, IMMEDIATE TELEPHONIC COMMUNICATION WITH LOCAL AND STATE HEALTH AUTHORITIES IS OBLIGATORY: CDC SHOULD BE CONTACTED ALSO. The CDC bioterrorism response coordination hotline is (770) 488-7100.

Specific treatment: Henderson DA, Inglesby TV, Bartlett JG, et al. Smallpox as a biological weapon: medical and public health management. JAMA 1999; 281 (22):2127-2137 (In *Additional resources*).